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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,249	12/17/2001	Manuel Vega	37851-911	7196

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EXAMINER	
LIN, JERRY	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,249	VEGA ET AL.	
	Examiner	Art Unit	
	Jerry Lin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 42-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,27-30,32,33 and 42-44* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page (6/22/06)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 22, 2006 has been entered.

Applicants' arguments, filed June 22, 2006, have been fully considered and they are deemed to be persuasive. However, in light of newly discovered art and the amendments, the following rejections and objections are newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1-33 and 42-44 are under examination.

Claims 34-41 are cancelled (drawn to an unelected invention).

Claim Objections

2. Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Instant claim 4 recites that

each polynucleotides in each set encodes a protein that differs by one amino acid. However, instant claim 1 recites that the modified nucleic acids encode a protein that differ by one amino acid from the target protein. Thus claim 4 does not further limit claim 1.

Claim Rejections - 35 USC § 112, 2nd Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-21, and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 includes the limitation of "the host cells are provided as an addressable array." This limitation is unclear since it seems to state that the cells themselves are an addressable array, rather than the cells are found in an addressable array or the cells are organized in an addressable array. Clarification via clearer language is requested.

6. Claims 14, 15, 43 and 44 recite the limitation "the codon." The parent claim contains both a codon in the target protein and a pre-selected codon. However it is unclear to which codon do the instant claims refer in the parent claim. Clarification via clearer language is requested.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-6, 8-23, 30, 32, 33, and 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Giver et al. (PNAS (1998) Volume 95, pages 12809-12813).

The instant claims are drawn to a method of identifying proteins with different properties by producing a set of nucleic acid molecules that encode modified proteins that differ from a target protein by one amino acid; introducing the nucleic acids into host cells on a array; expressing the proteins; screening the proteins for a chemical, physical, or biological property that differs from the target protein; and designating proteins with a different property from the target protein as a hit.

Regarding claims 1-6, 20 and 21, Giver et al. teach a method of producing sets of nucleic acids that encode for proteins that differ from the target protein by one amino acid (page 12809, right column, under Materials and Methods); introducing the nucleic acids into host cells (page 12810, left column, top paragraph) which were then placed into an addressable array (96 well plates) wherein each well had the same modified nucleic acid molecule (page 12810, left column top paragraph); expressing the proteins which differ from the target protein and modified proteins by one amino acid (page 12809, right column, under Materials and Methods; page 12810, left column); screening the proteins for a chemical, physical or biological property (page 12810); designating

each protein and its mutation with a different property as a hit (page 12810-12811; page 12812, left column bottom).

Regarding claim 8, Giver et al. teach wherein the host cells are bacterial cells and the nucleic acids comprise plasmids (page 12810, left column, top paragraph).

Regarding claims 9, 10, and 17-19 Giver et al. teach modifying the nucleic acids that encode modified hits and introducing those nucleic acids into cells and screening for a nucleic acid that encodes a protein with a predetermined property that differs from a target protein (page 12811, left column).

Regarding claim 11 and 12, Giver et al. teach using nucleic acid shuffling, recombination or random mutagenesis (page 12809, right column – page 12810, left column; page 12811, left column).

Regarding claim 13-16 and 42-44, Giver et al. teach wherein the codons are changed one by one (one amino acid substitution, site directed mutagenesis) to a codon that encodes Ala or Leu (page 12810, right column, bottom – page 12811, left column; page 12812, left column).

Regarding claims 22 and 23, Giver et al. teach wherein the proteins are now stable at a much higher temperature, thus there is stability at a temperature where there once was none. Since there is stability where there was once none, the change in activity would be at least 75% greater than the unmodified target protein (page 12810, right column, bottom – page 12811, left column).

Regarding claim 30, Giver et al. teach wherein the proteins are evaluated by fitting the output signal to a curve representative of the interaction of the target protein and a test compound (page 12810, Figure 1).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giver et al. (PNAS (1998) Volume 95, pages 12809-12813).

According to the MPEP Section 2106, Part VI, "merely using a computer to automate a known process does not by itself impart nonobviousness to the invention. *See Dann v. Johnston, 425 U.S. 219, 227-30, 189 USPQ 257, 261 (1976); In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958).*" Claims 32 and 33 are merely computer automations of claim 1. Thus, it would be obvious to one skilled in the art to use a computer to automate the known processes disclosed by Giver et al.

11. Claims 7, 24, and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giver et al. (PNAS (1998) Volume 95, pages 12809-12813) in view of Berlioz et al. (US 5,925,565).

The instant claims are drawn to a method of identifying proteins with different properties by producing a set of nucleic acid molecules that encode modified proteins that differ from a target protein by one amino acid; introducing the nucleic acids into host cells on a array; assessing the titer of viral vectors in each set of cells; expressing the proteins; screening the proteins for a chemical, physical, or biological property that differs from the target protein; and designating proteins with a different property from the target protein as a hit.

Giver et al. is applies as above.

However, Giver et al. does not teach using eukaryotic cells or assessing the titer of the viral vectors.

Berlioz et al. teaches assessing the titer of the viral vectors after transfection for each set of eukaryotic cells (column 14, lines 39-65) and where the viral vector encodes for a protein involved in viral replication (column 5, lines 35-65).

It would have been obvious at the time of the invention to combine the method taught by Berlioz et al. in Giver et al.'s method in order to study the effects of the protein in a eukaryotic setting. Berlioz et al. teaches a method that allows a eukaryotic cell such as a human cell to express a desired protein (column 6, lines 5-22) for the purpose of producing a therapeutic treatment (column 7, lines 15-25). Giver et al.'s method teaches screening for different proteins that exhibit the desired biological, chemical or physical properties (page 12810). The ability to manipulate these properties is important to create the desired therapeutic treatment. Thus one of ordinary skill in the art would be motivated to use Giver et al.'s method to design and screen for a desired

product and use Berlioz et al.'s method to express the protein for screening or production of the product. Thus it would have been obvious to one of ordinary skill in the art to combine the methods of Berlioz et al.

12. Claims 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giver et al. (PNAS (1998) Volume 95, pages 12809-12813), in view of Berlioz et al. (US 5,925,565), further in view of Rivet et al. (Gene therapy (2000) Volume 7, pages 924-929).

The instant claims are drawn to a method of identifying proteins with different properties by producing a set of nucleic acid molecules that encode modified proteins that differ from a target protein by one amino acid; introducing the nucleic acids into host cells on a array; assessing the titer of viral vectors in each set of cells; expressing the proteins; screening the proteins for a chemical, physical, or biological property that differs from the target protein; and designating proteins with a different property from the target protein as a hit. In particular the claims are drawn to method of determining the titer using real time virus titering and tagged replication and expression enhancement.

Giver et al. and Berlioz et al. are applied as above.

However Giver et al. and Berlioz et al. do not teach real-time virus titering or tagged replication and expression enhancement.

Regarding claims 25 and 26, Rivet et al. teaches real time virus titering (page 925) and using tagged replication and expression enhancement (page 926, right column).

It would have been obvious to one of ordinary skill in the art to combine the methods of Giver et al., Berlioz et al. and Rivet et al. in order to gain the benefit of determining the effectives of the viral vectors. Berlioz et al. teach that one his goals is to create a effective and stable viral vector (column 1, lines 10-17). Part of their method requires that they assess the titer of the viral vectors after transmission. Rivet et al.'s method provides further insight into the stability and efficacy of the vector by offering real time titering. Thus one or ordinary skill in the art would be motivated to combine the methods of Giver et al. and Berlioz et al. and Rivet et al. in order to gain the benefit of assessing the stability and efficacy of viral vectors more thoroughly.

13. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Giver et al. (PNAS (1998) Volume 95, pages 12809-12813), in view of Persson et al. (Journal of Virology (1985) Volume 54, pages 92-97).

The instant claims are drawn to a method of identifying proteins with different properties by producing a set of nucleic acid molecules that encode modified proteins that differ from a target protein by one amino acid; introducing the nucleic acids into host cells on a array; expressing the proteins; screening the proteins for a chemical, physical, or biological property that differs from the target protein; and designating proteins with a different property from the target protein as a hit. In particular the instant claims use Hill analysis.

Giver et al. is applied as above.

However Giver et al. do not teach using Hill analysis.

Persson et al. teach a method that uses the Hill analysis for determining the rate in which host cells are infected with viruses (abstract, page 94, left column).

It would have been obvious to one of ordinary skill in the art to combine the methods of Giver et al. and Persson et al. to gain the benefit of deterring if the plasmids or vectors are infecting the host cells. Giver et al. teach a method that creates host cells of desired nucleic acids. In such a method, it would be desirable to know the rate of infection in order to determine how to structure an experiment (e.g. incubation times, concentration, etc.). Persson et al. provide such a method of determining the rate. Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods of Giver et al. and Persson et al. to gain the benefit of determining the rate of infection of host cells.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00am-6:30pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Representatives are available to \ answer your questions daily from 6 am to midnight (EST). When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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